## **CLAIMS**

1. The use of a compound for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by a cyclin dependent kinase or glycogen synthase kinase-3 or an Aurora kinase, the compound having the formula (I):

or a salt, N-oxide or solvate thereof; wherein

10

5

X is CR<sup>5</sup> or N;

A is a bond or  $-(CH_2)_{m}-(B)_{n}$ ;

B is C=O,  $NR^g$ (C=O) or O(C=O) wherein  $R^g$  is hydrogen or  $C_{1-4}$  hydrocarbyl optionally substituted by hydroxy or  $C_{1-4}$  alkoxy;

m is 0, 1 or 2;

15

n is 0 or 1;

 $R^0$  is hydrogen or, together with  $NR^g$  when present, forms a group -( $CH_2$ )<sub>0</sub>- wherein p is 2 to 4;

R<sup>1</sup> is hydrogen, a carbocyclic or heterocyclic group having from 3 to 12 ring members, or an optionally substituted C<sub>1-8</sub> hydrocarbyl group;

20

R<sup>2</sup> is hydrogen, halogen, methoxy, or a C<sub>1-4</sub> hydrocarbyl group optionally substituted by halogen, hydroxyl or methoxy;

R<sup>3</sup> and R<sup>4</sup> together with the carbon atoms to which they are attached form an optionally substituted fused carbocyclic or heterocyclic ring having from 5 to 7 ring members of which up to 3 can be heteroatoms selected from N, O and S; and

25

R<sup>5</sup> is hydrogen, a group R<sup>2</sup> or a group R<sup>10</sup> wherein R<sup>10</sup> is selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino,

10

mono- or di- $C_{1-4}$  hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group  $R^a$ - $R^b$  wherein  $R^a$  is a bond, O, CO,  $X^1C(X^2)$ ,  $C(X^2)X^1$ ,  $X^1C(X^2)X^1$ , S, SO, SO<sub>2</sub>, NR<sup>c</sup>, SO<sub>2</sub>NR<sup>c</sup> or NR<sup>c</sup>SO<sub>2</sub>; and  $R^b$  is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a  $C_{1-8}$  hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the  $C_{1-8}$  hydrocarbyl group may optionally be replaced by O, S, SO, SO<sub>2</sub>, NR<sup>c</sup>,  $X^1C(X^2)$ ,  $C(X^2)X^1$  or  $X^1C(X^2)X^1$ ;

 $R^c$  is selected from hydrogen and  $C_{1-4}$  hydrocarbyl; and  $X^1$  is O, S or  $NR^c$  and  $X^2$  is =0, =S or = $NR^c$ .

- 2. The use according to claim 1 wherein the medicament is for the prophylaxis or treatment of a disease state or condition mediated by a cyclin dependent kinase or glycogen synthase kinase-3.
  - The use according to claim 1 wherein the medicament is for the prophylaxis or treatment of a disease state or condition mediated by an Aurora kinase.
- 20 4. The use according to any one of the preceding claims wherein X is N.
  - 5. The use according to any one of the preceding claims 4 wherein m is 0 or 1 (preferably 0), n is 1 and B is C=O.
  - 6. The use according to any one of the preceding claims wherein R<sup>0</sup> is hydrogen.
- 7. The use according to any one of the preceding claims wherein B is  $NR^g(C=0)$  and  $R^g$  is hydrogen.

WO 2005/002552 PCT/GB2004/002824

269

- 8. The use according to any one of the preceding claims wherein R<sup>1</sup> is a monocyclic or bicyclic carbocyclic or heterocyclic group having from 3 to 12 ring members, more preferably 3 to 10 ring members.
- 9. The use according to claim 8 wherein the carbocyclic or heterocyclic group is an aryl group.
  - 10. The use according to claim 8 wherein the carbocyclic or heterocyclic group is a heteroaryl group.
- 11. The use according to claim 9 or claim 10 wherein the aryl and heteroaryl groups are selected from pyrazolo[1,5-a]pyridinyl (e.g. pyrazolo[1,5-a]pyridin-3-yl), furanyl (e.g. 2-furanyl and 3-furanyl), indolyl (e.g. 3-indolyl, 4-indolyl and 7-indolyl), oxazolyl, thiazolyl (e.g. thiazol-2-yl and thiazol-5-yl), isoxazolyl (e.g. isoxazol-3-yl and isoxazol-4-yl), pyrrolyl (e.g. 3-pyrrolyl), pyridyl (e.g. 2-pyridyl), quinolinyl (e.g. quinolin-8-yl), 2,3-dihydro-benzo[1,4]dioxine (e.g. 2,3-dihydro-benzo[1,4]dioxine (e.g. 2,3-dihydrobenzofuranyl (e.g. 2,3-dihydrobenzofuran-7-yl), imidazolyl and thiophenyl (e.g. 3-thiophenyl) groups.
- 12. The use according to claim 11 wherein the aryl and heteroaryl groups are selected from substituted or unsubstituted phenyl, pyrazolo[1,5-a]pyridinyl, furanyl, 2,3-dihydrobenzofuranyl, thiophenyl, indolyl, thiazolyl, isoxazolyl and 2,3-dihydro-benzo[1,4]dioxine groups.
  - 13. The use according to claim 11 wherein the aryl and heteroaryl groups are selected from substituted or unsubstituted phenyl, furanyl, indolyl, oxazolyl, isoxazolyl, pyridyl, quinolinyl, 2,3-dihydro-benzo[1,4]dioxine, benzo[1,3]dioxole, imidazolyl and thiophenyl groups.

25

14. The use according to claim 12 wherein R<sup>1</sup> is a substituted or unsubstituted phenyl ring.

- 15. The use according to claim 8 wherein R<sup>1</sup> is a non-aromatic group selected from monocyclic cycloalkyl groups and azacycloalkyl groups such as cyclohexyl, cyclopentyl, and piperidinyl.
- The use according to any one of claims 8 to 15 wherein the carbocyclic or
   heterocyclic group R<sup>1</sup> is an unsubstituted group.
  - 17. The use according to any one of claims 8 to 15 wherein the carbocyclic or heterocyclic group R<sup>1</sup> bears one or more substituents selected from the group R<sup>10</sup> as defined in claim 1.
- The use according to claim 17 wherein the substituents on R<sup>1</sup> are selected 18. from the group R 10a consisting of halogen, hydroxy, trifluoromethyl, 10 cyano, nitro, carboxy, heterocyclic groups having 5 or 6 ring members and up to 2 heteroatoms selected from O, N and S, a group Ra-Rb wherein Ra is a bond, O, CO,  $X^3C(X^4)$ ,  $C(X^4)X^3$ ,  $X^3C(X^4)X^3$ , S, SO, or SO<sub>2</sub>, and  $R^b$  is selected from hydrogen, heterocyclic groups having 5 or 6 ring members and up to 2 heteroatoms selected from O, N and S, and a C<sub>1-8</sub> hydrocarbyl 15 group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di-C1-4 hydrocarbylamino, carbocyclic and heterocyclic groups having 5 or 6 ring members and up to 2 heteroatoms selected from O, N and S; wherein one or more carbon atoms of the C<sub>1-8</sub> hydrocarbyl group may optionally be 20 replaced by O, S, SO, SO<sub>2</sub>,  $X^3C(X^4)$ ,  $C(X^4)X^3$  or  $X^3C(X^4)X^3$ ;  $X^3$  is O or S; and  $X^4$  is =0 or =S.
- The use according to claim 18 wherein the substituents on R<sup>1</sup> are selected from the group R<sup>10b</sup> consisting of halogen, hydroxy, trifluoromethyl,
  cyano, nitro, carboxy, a group R<sup>a</sup>-R<sup>b</sup> wherein R<sup>a</sup> is a bond, O, CO, X<sup>3</sup>C(X<sup>4</sup>), C(X<sup>4</sup>)X<sup>3</sup>, X<sup>3</sup>C(X<sup>4</sup>)X<sup>3</sup>, S, SO, or SO<sub>2</sub>, and R<sup>b</sup> is selected from hydrogen and a C<sub>1-8</sub> hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy; wherein one or more carbon atoms of the C<sub>1-8</sub> hydrocarbyl group

may optionally be replaced by O, S, SO, SO<sub>2</sub>,  $X^3C(X^4)$ ,  $C(X^4)X^3$  or  $X^3C(X^4)X^3$ ;  $X^3$  is O or S; and  $X^4$  is =O or =S.

- The use according to claim 19 wherein the substituents on R<sup>1</sup> are selected from halogen, hydroxy, trifluoromethyl, a group R<sup>a</sup>-R<sup>b</sup> wherein R<sup>a</sup> is a bond or O, and R<sup>b</sup> is selected from hydrogen and a C<sub>1-4</sub> hydrocarbyl group optionally substituted by one or more substituents selected from hydroxyl and halogen.
  - 21. The use according to any one of claims 17 to 20 wherein R<sup>1</sup> is substituted by 1 or 2 or 3 or 4 substituents.
- The use according to claim 21 wherein R<sup>1</sup> is a phenyl group which is 2,6-disubstituted, 2,3-disubstituted, 2,4-disubstituted 2,5-disubstituted, 2,3,6-trisubstituted or 2,4,6-trisubstituted.
- The use according to claim 22 wherein R<sup>1</sup> is a phenyl group which is disubstituted at positions 2- and 6- with substituents selected from fluorine, chlorine and R<sup>a</sup>-R<sup>b</sup>, where R<sup>a</sup> is O and R<sup>b</sup> is C<sub>1-4</sub> alkyl.
  - 24. The use according to any one of the preceding claims wherein the compound is represented by the formula (II):

$$R^{1}$$
 $A$ 
 $NH$ 
 $R^{2}$ 
 $N$ 
 $H$ 
 $R^{8}$ 
 $R^{8}$ 
 $R^{1}$ 
 $R^{1}$ 
 $R^{1}$ 
 $R^{2}$ 
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{5}$ 
 $R^{7}$ 
 $R^{8}$ 
 $R^{1}$ 
 $R^{1}$ 
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{7}$ 
 $R^{8}$ 
 $R^{1}$ 
 $R^{1}$ 
 $R^{2}$ 
 $R^{3}$ 
 $R^{4}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{5}$ 
 $R^{5}$ 

wherein R<sup>1</sup>, R<sup>2</sup> and X are as defined in any one of the preceding claims;

Y is N or CR<sup>9</sup> wherein R<sup>9</sup> is hydrogen or a group R<sup>10</sup>; and

R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> are the same or different and each is hydrogen or a group

R<sup>10</sup> as defined in any one of the preceding claims.

25. The use according to claim 24 wherein the compound is represented by the formula (III):

wherein  $R^1$ ,  $R^2$  and  $R^6$  to  $R^9$  are as defined in any one of the preceding claims.

26. The use according to claim 24 wherein the compound is represented by the formula (IIIa):

wherein  $R^1$ ,  $R^2$  and  $R^6$  to  $R^9$  are as defined in the preceding claims.

10 27. A compound of the formula (IV):

or a salt, N-oxide or solvate thereof; wherein A is NH(C=O), O(C=O) or C=O;

10

15

20

25

30

R<sup>6a</sup>, R<sup>7a</sup>, R<sup>8a</sup> and R<sup>9a</sup> are the same or different and each is selected from hydrogen, halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di-C<sub>1-4</sub> hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group Ra-Rb wherein Ra is a bond, O, CO,  $X^1C(X^2)$ ,  $C(X^2)X^1$ ,  $X^1C(X^2)X^1$ , S, SO, SO<sub>2</sub>,  $NR^c$ ,  $SO_2NR^c$ or NR<sup>c</sup>SO<sub>2</sub>; and R<sup>b</sup> is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a C<sub>1-8</sub> hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, monoor di-C<sub>1-4</sub> hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C<sub>1-8</sub> hydrocarbyl group may optionally be replaced by O, S, SO, SO<sub>2</sub>, NR<sup>c</sup>,  $X^{1}C(X^{2})$ ,  $C(X^{2})X^{1}$  or  $X^{1}C(X^{2})X^{1}$ ; or two adjacent groups  $R^{6a}$ ,  $R^{7a}$ ,  $R^{8a}$  or R<sup>9a</sup> together with the carbon atoms to which they are attached may form a 5-membered heteroaryl ring or a 5- or 6-membered non-aromatic heterocyclic ring, wherein the said heteroaryl and heterocyclic groups contain up to 3 heteroatom ring members selected from N, O and S;

 $R^c$  is selected from hydrogen and  $C_{1-4}$  hydrocarbyl; and  $X^1$  is O, S or  $NR^c$  and  $X^2$  is =O, =S or = $NR^c$ ;

or an adjacent pair of substituents selected from  $R^{6a}$ ,  $R^{7a}$ ,  $R^{8a}$  and  $R^{9a}$  together with the carbon atoms to which they are attached may form a non-aromatic five or six membered ring containing up to three heteroatoms selected from O, N and S;  $R^{1a}$  is selected from:

- o 6-membered monocyclic aryl groups substituted by one to three substituents R<sup>10c</sup> provided that when the aryl group is substituted by a methyl group, at least one substituent other than methyl is present:
- o 6-membered monocyclic heteroaryl groups containing a single heteroatom ring member which is nitrogen, the heteroaryl groups being substituted by one to three substituents R<sup>10c</sup>;

15

20

- 5-membered monocyclic heteroaryl groups containing up to three heteroatom ring members selected from nitrogen and sulphur, and being optionally substituted by one to three substituents R<sup>10c</sup>;
- o 5-membered monocyclic heteroaryl groups containing a single oxygen heteroatom ring member and optionally a nitrogen heteroatom ring member, and being substituted by one to three substituents R<sup>10c</sup> provided that when the heteroaryl group contains a nitrogen ring member and is substituted by a methyl group, at least one substituent other than methyl is present;
- o bicyclic aryl and heteroaryl groups having up to four heteroatom ring members and wherein either one ring is aromatic and the other ring is non-aromatic, or wherein both rings are aromatic, the bicyclic groups being optionally substituted by one to three substituents R<sup>10c</sup>;
  - o four-membered, six-membered and seven-membered monocyclic C-linked saturated heterocyclic groups containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, the heterocyclic groups being optionally substituted by one to three substituents R<sup>10c</sup> provided that when the heterocyclic group has six ring members and contains only one heteroatom which is oxygen, at least one substituent R<sup>10c</sup> is present;
  - o five membered monocyclic C-linked saturated heterocyclic groups containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, the heterocyclic groups being optionally substituted by one to three substituents R<sup>10c</sup> provided that when the heterocyclic group has five ring members and contains only one heteroatom which is nitrogen, at least one substituent R<sup>10c</sup> other than hydroxy is present;
    - o four and six membered cycloalkyl groups optionally substituted by one to three substituents R<sup>10c</sup>;
    - o three and five membered cycloalkyl groups substituted by one to three substituents R<sup>10c</sup>; and
- o a group Ph'CR<sup>17</sup>R<sup>18</sup>- where Ph' is a phenyl group substituted by one to three substituents R<sup>10c</sup>; R<sup>17</sup> and R<sup>18</sup> are the same or different and each is

10

- selected from hydrogen and methyl; or  $R^{17}$  and  $R^{18}$  together with the carbon atom to which they are attached form a cyclopropyl group; or one of  $R^{17}$  and  $R^{18}$  is hydrogen and the other is selected from amino, methylamino,  $C_{1-4}$  acylamino, and  $C_{1-4}$  alkoxycarbonylamino; and where one of  $R^{6a}$ ,  $R^{7a}$ ,  $R^{8a}$  and  $R^{9a}$  is a morpholinomethyl group, then  $R^{1a}$  is additionally selected from:
- o unsubstituted phenyl and phenyl substituted with one or more methyl groups;
- o unsubstituted 6-membered monocyclic heteroaryl groups containing a single heteroatom ring member which is nitrogen;
- o unsubstituted furyl;
- 5-membered monocyclic heteroaryl groups containing a single oxygen heteroatom ring member and a nitrogen heteroatom ring member, and being unsubstituted or substituted by one or more methyl groups;
- o unsubstituted six membered monocyclic C-linked saturated heterocyclic groups containing only one heteroatom which is oxygen; and
  - o unsubstituted three and five membered cycloalkyl groups; and R<sup>10c</sup> is selected from:
  - o halogen (e.g. F and Cl);
- o hydroxyl;
  - o C<sub>1-4</sub> hydrocarbyloxy optionally substituted by one or more substituents selected from hydroxyl and halogen;
  - C<sub>1-4</sub> hydrocarbyl substituted by one or more substituents selected from hydroxyl, halogen and five and six-membered saturated heterocyclic rings containing one or two heteroatom ring members selected from nitrogen, oxygen and sulphur;
  - o S-C<sub>1-4</sub> hydrocarbyl;
  - o phenyl optionally substituted with one to three substituents selected from C<sub>1-4</sub> alkyl, trifluoromethyl, fluoro and chloro;
- o heteroaryl groups having 5 or 6 ring members (e.g. oxazole, pyridyl, pyrimidinyl) and containing up to 3 heteroatoms selected from N, O and

20

- S, the heteroaryl groups being optionally substituted with one to three substituents selected from C<sub>1-4</sub> alkyl, trifluoromethyl, fluoro and chloro;
- 5- and 6-membered non-aromatic heterocyclic groups (e.g. pyrrolidino, piperidino, piperazine, N-methylpiperazino, morpholino) containing up to 3 heteroatoms selected from N, O and S and being optionally substituted with one to three substituents selected from C<sub>1-4</sub> alkyl, trifluoromethyl, fluoro and chloro;
- o cyano, nitro, amino, C<sub>1-4</sub> alkylamino, di-C<sub>1-4</sub>alkylamino, C<sub>1-4</sub> acylamino, C<sub>1-4</sub> alkoxycarbonylamino;
- o a group R<sup>19</sup>-S(O)<sub>n</sub>- where n is 0, 1 or 2 and R<sup>19</sup> is selected from amino; C<sub>1-4</sub> alkylamino; di-C<sub>1-4</sub>alkylamino; C<sub>1-4</sub> hydrocarbyl; phenyl optionally substituted with one to three substituents selected from C<sub>1-4</sub> alkyl, trifluoromethyl, fluoro and chloro; and 5- and 6-membered non-aromatic heterocyclic groups containing up to 3 heteroatoms selected from N, O and S and being optionally substituted with one to three C<sub>1-4</sub> alkyl group substituents; and
  - o a group R<sup>20</sup>-Q- where R<sup>20</sup> is phenyl optionally substituted with one to three substituents selected from C<sub>1-4</sub> alkyl, trifluoromethyl, fluoro and chloro; and Q is a linker group selected from OCH<sub>2</sub>, CH<sub>2</sub>O, NH, CH<sub>2</sub>NH, NCH<sub>2</sub>, CH<sub>2</sub>, NHCO and CONH.
  - 28. A compound of the formula (V):

$$R^{1b}$$
  $A$   $NH$   $N$   $R^{6a}$   $R^{9a}$   $R^{7a}$   $R^{7a}$   $R^{8a}$   $R^{8a}$ 

or a salt, N-oxide or solvate thereof;

25 wherein
A is NH(C=O) or C=O;

10

15

20

R<sup>1b</sup> is a substituted phenyl group having from 1 to 4 substituents whereby:

- (i) when R<sup>1b</sup> bears a single substituent it is selected from halogen, hydroxyl, C<sub>1-4</sub> hydrocarbyloxy optionally substituted by one or more substituents selected from hydroxyl and halogen; C<sub>1-4</sub> hydrocarbyl substituted by one or more substituents selected from hydroxyl and halogen; heteroaryl groups having 5 ring members; and 5- and 6-membered non-aromatic heterocyclic groups, wherein the heteroaryl and heterocyclic groups contain up to 3 heteroatoms selected from N, O and S;
- (ii) when R<sup>1b</sup> bears 2, 3 or 4 substituents, each is selected from halogen, hydroxyl, C<sub>1-4</sub> hydrocarbyloxy optionally substituted by one or more substituents selected from hydroxyl and halogen; C<sub>1-4</sub> hydrocarbyl optionally substituted by one or more substituents selected from hydroxyl and halogen; heteroaryl groups having 5 ring members; amino; and 5- and 6-membered non-aromatic heterocyclic groups; or two adjacent substituents together with the carbon atoms to which they are attached form a 5-membered heteroaryl ring or a 5- or 6-membered non-aromatic heterocyclic ring; wherein the said heteroaryl and heterocyclic groups contain up to 3 heteroatoms selected from N, O and S; and R<sup>6a</sup>, R<sup>7a</sup>, R<sup>8a</sup> and R<sup>9a</sup> are as defined in claim 8.
- 29. A compound of the formula (Va):

10

15

or a salt, N-oxide or solvate thereof; wherein R<sup>6a</sup> to R<sup>9a</sup> are as defined in claim 8; and

- (i) R<sup>13</sup> is methoxy and R<sup>14</sup> to R<sup>16</sup> each are hydrogen; or
- (ii)  $R^{14}$  is oxazolyl, imidazolyl or thiazolyl, preferably oxazolyl, and  $R^{13}$ ,  $R^{15}$  and  $R^{16}$  each are hydrogen; or
- (iii) R<sup>13</sup> is selected from fluorine, chlorine and methyl, R<sup>16</sup> is selected from fluorine, chlorine, methyl and methoxy, and R<sup>14</sup> and R<sup>15</sup> each are hydrogen; or
- (iv) R<sup>13</sup> and R<sup>16</sup> each are selected from fluorine, chlorine and methyl; R<sup>14</sup> is selected from fluorine, chlorine, methyl and methoxy; and R<sup>15</sup> is hydrogen; or
- (v) R<sup>13</sup> and R<sup>14</sup> each are hydrogen; R<sup>15</sup> is selected from fluorine, chlorine, methyl and methoxy (more preferably methyl and methoxy), and R<sup>16</sup> is selected from fluorine, chlorine and methyl (more preferably fluorine), or R<sup>15</sup> and R<sup>16</sup> together with the carbon atoms of the phenyl ring form a group selected from:

30. A compound of the formula (VI):

or a salt, N-oxide or solvate thereof; wherein:
when A is NH(C=O) or C=O;

R<sup>1c</sup> is selected from:

10

15

20

25

30

(a) a mono-substituted phenyl group wherein the substituent is selected from o-amino, o-methoxy; o-chloro; p-chloro; o-difluoromethoxy; otrifluoromethoxy; o-tert-butyloxy; m-methylsulphonyl and p-fluoro; (b) a 2,4- or 2,6-disubstituted phenyl group wherein one substituent is selected from o-methoxy, o-ethoxy, o-fluoro, p-morpholino and the other substituent is selected from o-fluoro, o-chloro, p-chloro, and p-amino; (c) a 2,5-disubstituted phenyl group wherein one substituent is selected from o-fluoro and o-methoxy and the other substituent is selected from mmethoxy, m-isopropyl; m-fluoro, m-trifluoromethoxy, m-trifluoromethyl, m-methylsulphanyl, m-pyrrolidinosulphonyl, m-(4-methylpiperazin-1yl)sulphonyl, m-morpholinosulphonyl, m-methyl, m-chloro and maminosulphonyl; (d) a 2,4,6-tri-substituted phenyl group where the substituents are the same or different and are each selected from o-methoxy, o-fluoro, p-fluoro, pmethoxy provided that no more than one methoxy substituent is present; (e) a 2,4,5-tri-substituted phenyl group where the substituents are the same or different and are each selected from o-methoxy, m-chloro and p-amino; (f) unsubstituted benzyl; 2,6-difluorobenzyl; α,α-dimethylbenzyl; 1phenylcycloprop-1-yl; and α-tert-butoxycarbonylaminobenzyl; (g) an unsubstituted 2-furyl group or a 2-furyl group bearing a single substituent selected from 4-(morpholin-4-ylmethyl), piperidinylmethyl; and optionally a further substituent selected from methyl; (h) an unsubstituted pyrazolo[1,5-a]pyridin-3-yl group; (i) isoxazolyl substituted by one or two C<sub>1-4</sub> alkyl groups; (j) 4,5,6,7-tetrahydro-benz[d]isoxazol-3-yl; (k) 3-tert-butyl-phenyl-1H-pyrazol-5-vl: (l) quioxalinyl; (m) benz[c]isoxazol-3-yl; (n) 2-methyl-4-trifluoromethyl-thiazol-5-yl; (o) 3-phenylamino-2-pyridyl;

(p) 1-toluenesulphonylpyrrol-3-yl;

- (q) 2,4-dimethoxy-3-pyridyl; and 6-chloro-2-methoxy-4-methyl-3pyridyl; (r) imidazo[2,1-b]thiazol-6-yl; (s) 5-chloro-2-methylsulphanyl-pyrimidin-4-yl; 5 (t) 3-methoxy-naphth-2-yl; (u) 2,3-dihydro-benz[1,4]dioxin-5-yl: (v) 2,3-dihydro-benzfuranyl group optionally substituted in the five membered ring by one or two methyl groups; (w) 2-methyl-benzoxazol-7-yl; 10 (x) 4-aminocyclohex-1-yl; (y) 1,2,3,4-tetrahydro-quinolin-6-yl: (z) 2-methyl-4,5,6,7-tetrahydro-benzfuran3-yl; (aa) 2-pyrimidinyl-1piperidin-4-yl; and 1-(5-trifluoromethyl-2-pyridyl)piperidin-4-yl and 1-methylsulphonylpiperidin-4-yl; 15 (ab) 1-cyanocyclopropyl: (ac) N-benzylmorpholin-2-yl: and when A is NH(C=O), R1' is additionally selected from: (ad) unsubstituted phenyl; R<sup>9b</sup> is selected from hydrogen; chlorine; methoxy; methylsulphonyl; 4methyl-piperazin-1-ylcarbonyl; morpholinocarbonyl; morpholinomethyl; 20 pyrrolidinylcarbonyl; N-methyl-piperidinyloxy; pyrrolidinylethoxy; morpholinopropylaminomethyl; 4-cyclopentyl-piperazin-1-ylmethyl; 4ethylsulphonyl-piperazin-1-ylmethyl; morpholinosulphonyl; 4-(4methylcyclohexyl)-piperazin-1-ylmethyl; and R<sup>7b</sup> is selected from hydrogen; methyl; methoxy and ethoxy. 25
  - 31. A compound of the formula (VII):

or a salt, N-oxide or solvate thereof; wherein R<sup>1d</sup> is a group R<sup>1</sup>, R<sup>1a</sup>, R<sup>1b</sup>or R<sup>1c</sup> as defined in any one of the preceding claims.

32. A compound according to claim 31 having the formula (VIIa):

where R<sup>1d</sup> is as defined in claim 31.

33. A compound of the formula (VIII):

5

10

or a salt, N-oxide or solvate thereof;

where  $R^{1e}$  is a group  $R^{1a}$  or a group  $R^{1b}$  as defined in any one of the preceding claims.

34. A compound of the formula (IX):

WO 2005/002552 PCT/GB2004/002824

282

$$R^{1d}$$
 $A$ 
 $NH$ 
 $N$ 
 $N$ 
 $R^{21}$ 
 $R^{22}$ 
 $R^{22}$ 

or a salt, N-oxide or solvate thereof; wherein R<sup>1d</sup> is as defined, E is a bond, CH<sub>2</sub> or CH<sub>2</sub>CH<sub>2</sub>, R<sup>22</sup> is selected from hydrogen, halogen (e.g. fluorine or chlorine), and C<sub>1-2</sub> alkoxy (e.g methoxy), and R<sup>21</sup> is selected from hydrogen, C<sub>1-4</sub> alkyl (e.g. methyl), C<sub>1-4</sub> acyl, and C<sub>1-4</sub> alkoxycarbonyl

35. The use of compound as defined in any one of claims 27 to 34 for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by a cyclin dependent kinase, glycogen synthase kinase or Aurora kinase

5

- 36. A method of inhibiting a cyclin dependent kinase, glycogen synthase kinase or Aurora kinase which method comprises contacting the kinase with a kinase-inhibiting compound of the formula (I) as defined in any one of claims 1 to 34.
- A method of modulating a cellular process (for example cell division) by inhibiting the activity of a cyclin dependent kinase, glycogen synthase kinase or Aurora kinase using a compound of the formula (I) as defined in any one of claims 1 to 34.
- 38. A method for treating a disease or condition comprising or arising from abnormal cell growth in a mammal, which method comprises administering to the mammal a compound of formula (I) as defined in any

WO 2005/002552 PCT/GB2004/002824

283

one of claims 1 to 34 in an amount effective in inhibiting abnormal cell growth.

39. A method for treating a disease or condition comprising or arising from abnormal cell growth in a mammal, the method comprising administering to the mammal a compound of formula (I) as defined in any one of claims 1 to 34 in an amount effective to inhibit cdk1 or cdk2 activity.

5

- 40. A compound of the formula (I) as defined in any one of claims 1 to 34 for use in the prophylaxis or treatment of a disease state or condition mediated by glycogen synthase kinase-3.
- The use of a compound of the formula (I) as in any one of claims 1 to 34 for the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by glycogen synthase kinase-3.
  - 42. A method for the prophylaxis or treatment of a disease state or condition mediated by glycogen synthase kinase-3, which method comprises administering to a subject in need thereof a compound of the formula (I) as defined in any one of claims 1 to 34.
    - 43. A method of inhibiting glycogen synthase kinase-3, which method comprises contacting the kinase with a kinase-inhibiting compound of the formula (I) as defined in any one of claims 1 to 34.
- A method of modulating a cellular process (for example cell division) by inhibiting the activity of glycogen synthase kinase-3 using a compound of the formula (I) as defined in any one of claims 1 to 34
- 45. A method for treating a disease or condition comprising or arising from abnormal cell growth in a mammal, the method comprising administering to the mammal a compound of formula (I) as defined in any one of claims 1 to 34 in an amount effective to inhibit glycogen synthase kinase-3 activity.

- 46. A use or method as defined in any one of the preceding claims wherein the disease state or condition is selected from proliferative disorders such as cancers and conditions such as viral infections, autoimmune diseases and neurodegenerative diseases.
- A use or method according to claim 46 wherein the disease state is a cancer selected from breast cancer, ovarian cancer, colon cancer, prostate cancer, oesophageal cancer, squamous cancer, and non-small cell lung carcinomas.
- The use of a compound as defined in any one of claims 1 to 34 for the manufacture of a medicament for the treatment or prophylaxis of a fungal infection in an animal.
  - 49. A method for the treatment or prophylaxis of a fungal infection in an animal or plant comprising administering to the animal or plant an effective antifungal amount of a compound of the formula (I) as defined in any one of claims 1 to 34.
  - The use of a compound of the formula (I) as defined in any one of claims 1 to 34 for the manufacture of a medicament for prophylaxis or treatment of a disease or condition characterised by up-regulation of an Aurora kinase (e.g. Aurora A kinase or Aurora B kinase).
- 20 51. A method for the prophylaxis or treatment of (or alleviating or reducing the incidence of) a disease state or condition characterised by upregulation of an Aurora kinase (e.g. Aurora A kinase or Aurora B kinase); which method comprises (i) subjecting a patient to a diagnostic test to detect a marker characteristic of up-regulation of the Aurora kinase and (ii) where the diagnostic test is indicative of up-regulation of Aurora kinase, thereafter administering to the patient a compound of the formula (I) as defined in any one of claims 1 to 34 having Aurora kinase inhibiting activity.

- 52. A compound as defined in any one of claims 27 to 34 for use in medicine.
- A pharmaceutical composition comprising a compound as defined in any one of claims 27 to 34 and a pharmaceutically acceptable carrier.
- A process for the preparation of a compound as defined in any one of claims 1 to 34, which process comprises:
  - (i) the reaction of a compound of the formula:

with a compound of the formula R<sup>1</sup>-A' wherein A' is an isocyanate group N=C=O, or a group CO<sub>2</sub>H or an activated derivative thereof; or

10 (ii) the reaction of a compound of the formula:

with a diamine compound of the formula:

$$H_2N$$
 $R^3$ 
 $H_2N$ 

wherein R<sup>1</sup>, A, R<sup>3</sup> and R<sup>4</sup> are as defined in any one of the preceding claims; and optionally thereafter converting one compound of the formula (I) into another compound of the formula (I).